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UserID: NOgihara
Computer: WS11333
Date: 06/12/2000
Time: 17:29

	Type		Search Text
1	BRS	17142	((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID))
2	BRS	1481	((((LBD OR RECEPTOR?) OR (LIGAND ADJ BINDING ADJ DOMAINS)) NEAR5 ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)))
3	BRS	723	((CO-ACTIVATORS OR COACTIVATORS))
4	BRS	2876572	((MODELING OR MODEL OR STRUCTURAL OR CRYSTAL OR STRUCTURE))
5	BRS	20	((((CO-ACTIVATORS OR COACTIVATORS)) AND (((LBD OR RECEPTOR?) OR (LIGAND ADJ BINDING ADJ DOMAINS)) NEAR5 ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)))) AND ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)) AND ((MODELING OR MODEL OR STRUCTURAL OR CRYSTAL OR STRUCTURE)))
6	BRS	150364	((MODELING OR MODEL) AND (STRUCTURAL OR CRYSTAL OR STRUCTURE))
7	BRS	8	((((CO-ACTIVATORS OR COACTIVATORS)) AND (((LBD OR RECEPTOR?) OR (LIGAND ADJ BINDING ADJ DOMAINS)) NEAR5 ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)))) AND ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)) AND ((MODELING OR MODEL) AND (STRUCTURAL OR CRYSTAL OR STRUCTURE))))
8	BRS	2619	((TRANSCRIPTIONS NEAR5 (ACTIVATORS OR ACTIVATION))

	DBs	Time Stamp	Comments	Error Definition
1	USPAT; EPO; JPO; Derwent	2000/06/12 12:50		
2	USPAT; EPO; JPO; Derwent	2000/06/12 13:03		
3	USPAT; EPO; JPO; Derwent	2000/06/12 12:52		
4	USPAT; EPO; JPO; Derwent	2000/06/12 13:05		
5	USPAT; EPO; JPO; Derwent	2000/06/12 13:07		
6	USPAT; EPO; JPO; Derwent	2000/06/12 13:07		
7	USPAT; EPO; JPO; Derwent	2000/06/12 13:17		
8	USPAT; EPO; JPO; Derwent	2000/06/12 13:18		

	Errors
1	0
2	0
3	0
4	0
5	0
6	0
7	0
8	0

	Type	Hits	Search Text
9	BRS	156	(((((LBD OR RECEPTOR?) OR (LIGAND ADJ BINDING ADJ DOMAINS)) NEAR5 ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)))) AND ((TRANSCRIPTIONS NEAR5 (ACTIVATORS OR ACTIVATION)))) AND ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)) AND ((MODELING OR MODEL) AND (STRUCTURAL OR CRYSTAL OR STRUCTURE))))
10	BRS	1361	(TRANSCRIPTIONS NEAR5 ACTIVATORS)
11	BRS	60	(((((TRANSCRIPTIONS NEAR5 ACTIVATORS)) AND (((LBD OR RECEPTOR?) OR (LIGAND ADJ BINDING ADJ DOMAINS)) NEAR5 ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)))) AND ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)) AND ((MODELING OR MODEL) AND (STRUCTURAL OR CRYSTAL OR STRUCTURE))))
12	BRS	0	(((((TRANSCRIPTIONS NEAR5 ACTIVATORS)) AND (((LBD OR RECEPTOR?) OR (LIGAND ADJ BINDING ADJ DOMAINS)) NEAR5 ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)))) AND ((ICOSANOID OR MINERALCORTICOID OR PEROXISOME OR PROGESTIN OR ESTROGEN OR ANDROGEN OR GLUCOCORTICOID OR RETINOID OR THYROID)) AND ((MODELING OR MODEL) AND (STRUCTURAL OR CRYSTAL OR STRUCTURE)))) and lxxll
13	BRS	7	lxxll

	DBs	Time Stamp	Comments	Error Definition
9	USPAT; EPO; JPO; Derwent	2000/06/12 13:18		
10	USPAT; EPO; JPO; Derwent	2000/06/12 13:18		
11	USPAT; EPO; JPO; Derwent	2000/06/12 13:46		
12	USPAT; EPO; JPO; Derwent	2000/06/12 13:46		
13	USPAT; EPO; JPO; Derwent	2000/06/12 13:46		

	Errors
9	0
10	0
11	0
12	0
13	0

=> a thyroid or retinoid or peroxisome or glucocorticoid or progestin or mineralcorticoid or androgen or estrogen or icosanoid

6 FILES SEARCHED...

L1 1051565 THYROID OR RETINOID OR PEROXISOME OR GLUCOCORTICOID OR PROGESTIN OR MINERALCORTICOID OR ANDROGEN OR ESTROGEN OR ICOSANOID

=> a receptor? or lbd or (ligand (w) binding (w) domain?)

4 FILES SEARCHED...

L2 2756052 RECEPTOR? OR LBD OR (LIGAND (W) BINDING (W) DOMAIN?)

SEARCH ENDED BY USER

=> s 11 (s) 12

L3 225402 L1 (S) L2

=> a fletterick r7/au

L4 1121 FLETTERICK R7/AU

=> s 13 and 14

L5 72 L3 AND L4

=>

=> s structur? or crystal

L6 6643763 STRUCTURE? OR CRYSTAL

=> s 15 and 16

L7 66 L5 AND L6

=> s structure (5w) drug (5w) design?

4 FILES SEARCHED...

L8 1868 STRUCTURE (5W) DRUG (5W) DESIGN?

=> s 17 and 18

L9 0 L7 AND L8

=> s 14 and (hormone (7w) receptor? (7w) thyroid)

3 FILES SEARCHED...

L10 12 L4 AND (HORMONE (7W) RECEPTOR? (7W) THYROID)

=> dup rem l10

PROCESSING COMPLETED FOR L10

L11 9 DUP REM L10 (3 DUPLICATES REMOVED)

=> d ti au so kwic 1-9

L11 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2000 ACS

TI Nuclear thyroid receptor ligand modeling based on three-dimensional structures of their ligand-binding domains

IN Scanlan, Thomas S.; Baxter, John D.; Fletterick, Robert J.; Wagner, Richard L.; Kushner, Peter J.; Apriletti, James W.; West, Brian L.; Shiau, Andrew K.
SO PCT Int. Appl., 447 pp.
CODEN: PIXXD2

IN Scanlan, Thomas S.; Baxter, John D.; Fletterick, Robert J.; Wagner, Richard L.; Kushner, Peter J.; Apriletti, James W.; West, Brian L.; Shiau, Andrew K.

IT Thyroid ***hormone*** ***receptors***
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)

(.alpha.-nuclear ***thyroid*** receptor ligand modeling based on three-dimensional structures of their ligand-binding domains)
IT Thyroid ***hormone*** ***receptors***

AU Clifton-Bligh, R. J.; De Zegher, F.; Wagner, R. L.; Collingwood, T. N.; Francois, I.; Van Helvoirt, M.; Fletterick, R. J.; Chatterjee, V. K. K.

IT Missense mutation
(R383H) thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Promoter (genetic element)
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
(TSH.alpha. and TRH: thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Thyroid ***hormones***
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(metabolic disorders, resistance syndrome; thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Transcriptional activation
Transcriptional repression
(thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Thyroid ***hormone*** ***receptor*** .beta.
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(***thyroid*** ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Retinoid X receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Endocrine diseases
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(thyroid ***hormone*** resistance syndrome; thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT 24305-27-9, Thyrotropin-releasing ***hormone***
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene promoter; thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT 6893-02-3, Triiodothyronine
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT 9002-71-5, Thyrotropin
RL: BSU (Biological study, unclassified); BIOL (Biological study)

RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)

(.beta.-nuclear ***thyroid*** receptor ligand modeling based on three-dimensional structures of their ligand-binding domains)
IT 51-24-ID, complex with ligand-binding domain of thyroid ***hormone*** ***receptors*** .alpha. and .beta. 6893-02-3D, 3,5,3'-Triiodothyronine, complex with ligand-binding domain of thyroid ***hormone*** ***receptors*** .alpha. and .beta. 13724-85-ID, complex with ligand-binding domain of thyroid ***hormone*** ***receptors*** .alpha. and .beta. 26384-44-ID, 3,5-Dimethyl-3'-isopropylthyronine, complex with ligand-binding domain of thyroid ***hormone*** ***receptors*** .alpha. and .beta. 21110-63-3D, complex with ligand-binding domain of thyroid ***hormone*** ***receptors*** .alpha. and .beta. 226082-39-9D, ligand complexes 226082-42-4D, ligand complexes 226082-43-5D, ligand complexes
RL: BPR (Biological process); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
(nuclear ***thyroid*** receptor ligand modeling based on three-dimensional structures of their ligand-binding domains)

L11 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2000 ACS

TI Molecular and structural biology of thyroid hormone receptors

AU Apriletti, James W.; Ribeiro, Ralf C. J.; Wagner, Richard L.; Feng, Weijun; Webb, Paul; Kushner, Peter J.; West, Brian L.; Nilsson, Stefan; Scanlan, Thomas S.; Fletterick, Robert J.; Baxter, John D.
SO Clin. Exp. Pharmacol. Physiol. (1998), 25(Suppl., Future Perspectives in Molecular Endocrinology), S2-S11
CODEN: CEXPB9; ISSN: 0305-1870

AU C. J.; Wagner, Richard L.; Feng, Weijun; Webb, Paul; Kushner, Peter J.; West, Brian L.; Nilsson, Stefan; Scanlan, Thomas S.; Fletterick, Robert J.; Baxter, John D.

IT Thyroid ***hormone*** ***receptors***
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)

(***thyroid*** hormone receptor mol. and structural biol.)

L11 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2000 ACS

TI Structure and specificity of nuclear receptor-coactivator interactions

AU Darimont, Beatrice D.; Wagner, Richard L.; Apriletti, James W.; Stallcup, Michael R.; Kushner, Peter J.; Baxter, John D.; Fletterick, Robert J.; Yamamoto, Keith R.

SO Genes Dev. (1998), 12(21), 3343-3356
CODEN: GEDEEP; ISSN: 0890-9369

AU Darimont, Beatrice D.; Wagner, Richard L.; Apriletti, James W.; Stallcup, Michael R.; Kushner, Peter J.; Baxter, John D.; Fletterick, Robert J.; Yamamoto, Keith R.

IT Thyroid ***hormone*** ***receptor*** .beta.
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(structure and specificity of ***thyroid*** hormone receptor-coactivator GRIP1 interactions)

L11 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2000 ACS

TI A novel TR.beta. mutation (R383H) in resistance to thyroid hormone syndrome predominantly impairs corepressor release and negative transcriptional regulation

AU Clifton-Bligh, R. J.; De Zegher, F.; Wagner, R. L.; Collingwood, T. N.; Francois, I.; Van Helvoirt, M.; Fletterick, R. J.; Chatterjee, V. K. K.

SO Mol. Endocrinol. (1998), 12(5), 609-621
CODEN: MOENEN; ISSN: 0888-8809

(.alpha.-subunit gene promoter: thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

L11 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2000 ACS

TI Mechanisms of thyroid hormone action: insights from X-ray crystallographic and functional studies

AU Ribeiro, Ralf C. J.; Apriletti, James W.; Wagner, Richard L.; West, Brian L.; Feng, Weijun; Huber, Russ; Kushner, Peter J.; Nilsson, Stefan; Scanlan, Thomas S.; Fletterick, Robert J.; Schaufele, Fred; Baxter, John D.

SO Recent Prog. Horm. Res. (1998), Volume Date 1997, 53, 351-394
CODEN: RPHRA6; ISSN: 0079-9963

AU Apriletti, James W.; Wagner, Richard L.; West, Brian L.; Feng, Weijun; Huber, Russ; Kushner, Peter J.; Nilsson, Stefan; Scanlan, Thomas S.; Fletterick, Robert J.; Schaufele, Fred; Baxter, John D.

IT Thyroid ***hormone*** ***receptors***
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)

(***thyroid*** hormone mechanism insights from X-ray crystallog. and functional studies)

L11 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2000 ACS

TI X-ray crystallographic and functional studies of thyroid hormone receptor

AU Ribeiro, Ralf C. J.; Apriletti, James W.; Wagner, Richard L.; Feng, Weijun; Kushner, Peter J.; Nilsson, Stefan; Scanlan, Thomas S.; West, Brian L.; Fletterick, Robert J.; Baxter, John D.

SO J. Steroid Biochem. Mol. Biol. (1998), 65(1-6), 133-141
CODEN: JSBBEZ; ISSN: 0960-0760

AU J.; Apriletti, James W.; Wagner, Richard L.; Feng, Weijun; Kushner, Peter J.; Nilsson, Stefan; Scanlan, Thomas S.; West, Brian L.; Fletterick, Robert J.; Baxter, John D.

IT Thyroid ***hormone*** ***receptors***
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)

(X-ray crystallog. and functional studies of ***thyroid*** hormone receptor)

L11 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2000 ACS

TI A natural transactivation mutation in the thyroid hormone .beta. receptor: impaired interaction with putative transcriptional mediators

AU Collingwood, T. N.; Rajanayagam, O.; Adams, M.; Wagner, R.; Cavailles, V.; Kalkhoven, E.; Matthews, C.; Nystrom, E.; Stenlof, K.; Lindstedt, G.; Tisell, L.; Fletterick, R. J.; Parker, M. G.; Chatterjee, V. K. K.

SO Proc. Natl. Acad. Sci. U. S. A. (1997), 94(1), 248-253
CODEN: PNASA6; ISSN: 0027-8424

AU Rajanayagam, O.; Adams, M.; Wagner, R.; Cavailles, V.; Kalkhoven, E.; Matthews, C.; Nystrom, E.; Stenlof, K.; Lindstedt, G.; Tisell, L.; Fletterick, R. J.; Parker, M. G.; Chatterjee, V. K. K.

IT Thyroid ***hormone*** .beta.
RL: BPR (Biological process); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(natural transactivation mutation in ***thyroid*** hormone .beta. receptor with impaired interaction with putative transcriptional mediators)

L11 ANSWER 8 OF 9 MEDLINE DUPLICATE 1

TI A structural role for hormone in the thyroid hormone receptor.

AU Wagner R L; Apriletti J W; McGrath M E; West B L; Baxter J D;

Fletterick R J
 SO NATURE, (1995 Dec 14) 378 (6558) 690-7.
 Journal code: NSC. ISSN: 0028-0936.
 AU Wagner R L; Apriletti J W; McGrath M E; West B L; Baxter J D;
 Fletterick R J
 AB The crystal structure of the rat alpha 1 thyroid hormone receptor***
 receptor ligand-binding domain bound with a ***thyroid***
 hormone agonist reveals that ligand is completely buried within the domain
 as part of the hydrophobic core. In addition, the . . .

L11 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2000 ACS
 TI The molecular biology of thyroid hormone action
 AU Ribeiro, Ralf C. J.; Apriletti, James W.; West, Brian L.; Wagner, Richard
 L.; ***Fletterick, Robert J.***; Schaufele, Fred; Baxter, John D.
 SO Ann. N. Y. Acad. Sci. (1995), 758 (DNA: The Double Helix), 366-89
 CODEN: ANYAAS; ISSN: 0077-8523
 AU Ribeiro, Ralf C. J.; Apriletti, James W.; West, Brian L.; Wagner, Richard
 L.; ***Fletterick, Robert J.***; Schaufele, Fred; Baxter, John D.
 AB A review, with 99 refs., of thyroid hormone action which discusses:
 historical and general aspects of thyroid hormone receptors; the
 nuclear hormone receptor superfamily; nuclear hormone receptor
 hormone ***receptor*** function; characteristics of
 thyroid hormone receptors; properties of TRs purified from natural
 sources; target gene recognition by TRs; heterodimerization of TRs with
 nuclear hormone.
 IT Thyroid ***hormone*** ***receptors***
 RI: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (***thyroid*** hormone action mol. biol.)

L11 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2000 ACS
 AN 1999:355792 CAPLUS
 DN 131:14490
 TI Nuclear thyroid receptor ligand modeling based on three-dimensional
 structures of their ligand-binding domains
 IN Scanlan, Thomas S.; Baxter, John D.; ***Fletterick, Robert J.***;
 Wagner, Richard L.; Kushner, Peter J.; Apriletti, James W.; West, Brian
 L.; Shiao, Andrew K.
 PA The Regents of the University of California, USA
 SO PCT Int. Appl., 447 pp.
 CODEN: PIXX02
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926966	A2	19990603	WO 1998-US25296	19981125
WO 2000026966	A3	20000120		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
 DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
 KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
 NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
 UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM,
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9917999 A1 19990615 AU 1999-17999 19981125
 PRAI US 1997-980115 19971126
 WO 1998-US25296 19981125
 OS MARPAT 131:14490

the motif modulate the affinity of the interaction; the motif and the
 adjacent sequences are employed to different extents in binding to
 different receptors. Such interactions of amphipathic .alpha.-helices
 with hydrophobic grooves define protein interfaces in other regulatory
 complexes as well. We suggest that these common structural elements
 impart flexibility to combinatorial regulation, whereas side chains at the
 interface impart specificity.

L11 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2000 ACS
 TI A novel TR.beta. mutation (R383H) in resistance to thyroid hormone
 syndrome predominantly impairs corepressor release and negative
 transcriptional regulation
 AU Clifton-Bligh, R. J.; De Zegher, F.; Wagner, R. L.; Collingwood, T. N.;
 Francois, I.; Van Helvoirt, M.; ***Fletterick, R. J.***; Chatterjee,
 V. K. K.
 SO Mol. Endocrinol. (1998), 12(5), 609-621
 CODEN: MOENEN; ISSN: 0898-8809
 AB Resistance to thyroid hormone (RTH) is characterized by elevated serum
 thyroid hormones, failure to suppress pituitary TSH secretion, and
 variable T3 responsiveness in peripheral tissues. The disorder is assocd.
 with diverse mutations that cluster within three areas of the thyroid
 hormone .beta. (TR.beta.) receptor. Here, the authors report a novel RTH
 mutation (R383H), which is located in a region not known to harbor
 naturally occurring mutations. Although the R383H mutant receptor
 activated pos. regulated genes to an extent comparable to wild-type (WT),
 neg. transcriptional regulation of human TSH.alpha. and TRH promoters was
 impaired in either TR.beta.1 or TR.beta.2 contexts, and WT receptor
 function was dominantly inhibited. T3-dependent changes in basal
 transcription with R383H were also impaired: on the TRH promoter, basal
 activation by unliganded R383H was not reversed by T3 to the same extent
 as WT; similarly transcriptional silencing by an unliganded Gal4-R383H
 fusion was not relieved at a T3 concn. that derepressed WT. In keeping
 with this, ligand-dependent corepressor release by R383H, either in a
 protein-protein interaction assay or as a DNA-bound heterodimer with
 retinoid X receptor on either pos. or neg. thyroid hormone response
 elements, was disproportionately impaired relative to its ligand-binding
 affinity, whereas its T3-dependent recruitment of coactivator was
 unimpaired. These properties were shared by another previously described
 RTH mutant (R429Q), and in the crystal structure of TR.alpha. the
 homologous residues interact in a polar invagination. The authors' data
 indicate a role for these residues in mediating neg. transcriptional
 regulation and facilitating corepressor release and suggest that
 predominant impairment of these functions may be the minimal requirements
 for causation of RTH.

L11 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2000 ACS
 TI Mechanisms of thyroid hormone action: insights from X-ray crystallographic
 and functional studies
 AU Ribeiro, Ralf C. J.; Apriletti, James W.; Wagner, Richard L.; West, Brian
 L.; Feng, Weijun; Huber, Russ; Kushner, Peter J.; Nilsson, Stefan;
 Scanlan, Thomas; ***Fletterick, Robert J.***; Schaufele, Fred; Baxter,
 John D.
 SO Recent Prog. Horm. Res. (1998), Volume Date 1997, 53, 351-394
 CODEN: RPHRA6; ISSN: 0079-9963
 AB A review, with .apprx.200 refs., on the mechanisms of thyroid hormone
 action over the past two decades. We have attempted to place our studies
 on thyroid hormone receptors (TRs) in perspective with the work conducted
 by other investigators that established their nuclear localization,
 DNA-binding properties, DNA response elements, and the role of other
 proteins involved in TR-mediated regulation of gene transcription.
 Recently, our crystallog. studies of the TR ligand binding domain (LBD)

=> d t i au so abs 2-7

L11 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2000 ACS
 TI Molecular and structural biology of thyroid hormone receptors
 AU Apriletti, James W.; Ribeiro, Ralf C. J.; Wagner, Richard L.; Feng,
 Weijun; Webb, Paul; Kushner, Peter J.; West, Brian L.; Nilsson, Stefan;
 Scanlan, Thomas S.; ***Fletterick, Robert J.***; Baxter, John D.
 SO Clin. Exp. Pharmacol. Physiol. (1998), 25(Suppl., Future Perspectives in
 Molecular Endocrinology), S2-S11
 CODEN: CEXPB9; ISSN: 0305-1870
 AB A review, with 45 refs. Thyroid hormone receptors (TR) are expressed from
 two sep. genes (.alpha. and .beta.) and belong to the nuclear receptor
 superfamily, which also contains receptors for steroids, vitamins and
 prostaglandins. Unliganded TR are bound to DNA thyroid hormone response
 elements (TRE) predominantly as homodimers, or as heterodimers with
 retinoid X-receptors (RXR), and are assocd. with a complex of proteins
 contg. corepressor proteins. Ligand binding promotes corepressor dissonc.
 and binding of a coactivator. Recent studies from our group have focused
 on the acquisition and use of X-ray crystallog. structures of
 ligand-binding domains (LBD) of both the rat (r) TR.alpha. and the human
 (h) TR.beta. bound to several different ligands. We have also developed
 ligands that bind selectively to the TR.beta., which may provide ways to
 explore the differential functions of TR.alpha. compared with TR.beta.
 isoforms. The LBD is comprised mostly of .alpha.-helices. The ligand is
 completely buried in the receptor and forms part of its hydrophobic core.
 Kinetic studies suggest that the limiting step in formation of
 high-affinity ligand-receptor complexes is the rate of folding of the
 receptor around the ligand. Ligands can be fitted tightly in the
 ligand-binding pocket and small differences in this fitting may explain
 many structure-activity relationships. Interestingly, anal. of the
 structures of antagonists suggests that they have chem. groups,
 "extensions", that could impair receptor folding around them and, thus,
 prevent the agonist-induced conformation changes in the receptor. The TR
 structures allowed us to see that the mutations that occur in the syndrome
 of generalized resistance to thyroid hormone are located in the vicinity
 of the ligand-binding pocket. X-ray structure of the TR has also been
 used to guide the construction of mutations in the TR surface that block
 binding of various proteins important for receptor function. Studies with
 these TR mutants reveal that the interfaces for homo- and
 heterodimerization map to similar residues in helix 10 and 11 and also
 allow the definition of the surface for binding of coactivators, which
 appears to be general for nuclear receptors. Formation of this surface,
 which involves packing of helix 12 of the TR into a scaffold formed by
 helices 3 and 5, appears to be the major change in the receptor structure
 induced by hormone occupancy.

L11 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2000 ACS
 TI Structure and specificity of nuclear receptor-coactivator interactions
 AU Darimont, Beatrice D.; Wagner, Richard L.; Apriletti, James W.; Stallcup,
 Michael R.; Kushner, Peter J.; Baxter, John D.; ***Fletterick, Robert***
 J.***; Yamamoto, Keith R.
 SO Genes Dev. (1998), 12(21), 3343-3356
 CODEN: GEDEEP; ISSN: 0890-9369
 AB Combinatorial regulation of transcription implies flexible yet precise
 assembly of multiprotein regulatory complexes in response to signals.
 Biochem. and crystallog. anal. revealed that hormone binding leads to the
 formation of a hydrophobic groove within the ligand-binding domain (LBD)
 of the thyroid hormone receptor that interacts with an LXXLL motif-contg.
 .alpha.-helix from GRIP1, a coactivator. Residues immediately adjacent to

revealed that the ligand has a structural role in the folding of the
 receptor's hydrophobic core. The anal. of the structure led to biochem.
 and genetic studies that have defined the surfaces on the TR LBD required
 for dimerization and binding of coactivator proteins. Placement of the
 mutations found in patients with the syndrome of generalized resistance to
 thyroid hormone on the TR LBD revealed that they were restricted to amino
 acids in the vicinity of the binding pocket for thyroid hormone. The
 insights gained from the elucidation of the TR LBD structure will provide
 the basis for the design of compds. with selective agonistic or
 antagonistic activities.

L11 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2000 ACS
 TI X-ray crystallographic and functional studies of thyroid hormone receptor
 AU Ribeiro, Ralf C. J.; Apriletti, James W.; Wagner, Richard L.; Feng,
 Weijun; Kushner, Peter J.; Nilsson, Stefan; Scanlan, Thomas S.; West,
 Brian L.; ***Fletterick, Robert J.***; Baxter, John D.
 SO J. Steroid Biochem. Mol. Biol. (1998), 65(1-6), 133-141
 CODEN: JSBEEZ; ISSN: 0960-0760
 AB A review with 28 refs. We have solved several X-ray crystallog.
 structures of TR ligand-binding domains (LBDs), including the rat (r)
 TR.alpha. and the human (h) TR.beta. bound to diverse ligands. The TR-LBD
 folding, comprised mostly of .alpha.-helices, is likely to be general for
 the superfamily. The ligand, buried in the receptor, forms part of its
 hydrophobic core. Tight fitting of ligand into the receptor explains its
 high affinity for the TR, although the structure suggests that ligands
 with even higher affinities might be generated. The kinetics of
 3,5,3'-triiodo-L-thyronine (T3) and 3,5,3',5'-tetraiodo-L-thyronine (T4)
 binding suggest that folding around the ligand, rather than receptor
 opening, is rate-limiting for high affinity binding. TR.beta. mutations
 in patients with resistance to T3 cluster around the ligand; these
 different locations could differentially affect other receptor functions
 and explain the syndrome's clin. diversity. Guided by the structure,
 mutations have been placed on the TR surface to define interactions with
 other proteins. They suggest that a similar surface in the LBD is
 utilized for homo- or heterodimerization on direct repeats and inverted
 palindromes but not on palindromes. Coactivator proteins that mediate TR
 transcriptional activation bind to a small surface comprised of residues
 on four helices with a well-defined hydrophobic cleft, which may be a
 target for pharmaceuticals. The coactivator-binding surface appears to
 form upon ligand-binding by the folding of helix 12 into the scaffold
 formed by helices 3, 4 and 5. The anal. of most currently used
 antagonists suggest that although they probably fit into the
 ligand-binding pocket, they possess a group that may alter proper folding
 of the receptor, with disruption of the coactivator-binding surface (the
 "extension model").

L11 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2000 ACS
 TI A natural transactivation mutation in the thyroid hormone .beta. receptor:
 impaired interaction with putative transcriptional mediators
 AU Collingwood, T. N.; Rajanayagam, O.; Adams, M.; Wagner, R.; Cavailles, V.;
 Kalkhoven, E.; Matthews, C.; Nystrom, E.; Stenof, K.; Lindstedt, G.;
 Tisel, L.; ***Fletterick, R. J.***; Parker, M. G.; Chatterjee, V. K. K.
 SO Proc. Natl. Acad. Sci. U. S. A. (1997), 94(1), 240-253
 CODEN: PNASAG; ISSN: 0027-8424
 AB The syndrome of resistance to thyroid hormone is characterized by elevated
 serum free thyroid hormones, failure to suppress pituitary TSH secretion,
 and variable peripheral refractoriness to hormone action. Here we
 describe a novel leucine to valine mutation in codon 454 (L454V) of the
 thyroid hormone .beta. receptor (TR.beta.) in this disorder, resulting in
 a mutant receptor with unusual functional properties. Although the mutant

protein binds ligand comparably to wild-type receptor and forms homo- and heterodimers on direct repeat, inverted repeat, or palindromic thyroid response elements, its ability to activate transcription via these elements is markedly impaired. The hydrophobic leucine residue lies within an amphipathic .alpha.-helix at the C-terminus of TR.beta. and the position of the homologous residue in the crystal structure of TR.alpha. indicates that its side chain is solvent-exposed and might interact with other proteins. We find that two putative transcriptional mediators (RIP140 and SRC-1) exhibit hormone-dependent assocn. with wild-type TR. In comparison, the interaction of this natural mutant (L454V) and artificial mutants (L454A, E457A) with RIP140 and SRC-1 is markedly reduced. Furthermore, coexpression of SRC-1 is able to restore the transcriptional activity of the L454V mutant receptor, indicating that the interaction of this residue with accessory proteins is crit. for transcriptional activation. Finally, the occurrence of the L454V mutation in resistance to thyroid hormone, together with impaired neg. regulation of the TSH .alpha. promoter by this mutant, suggests that the amphipathic .alpha.-helix also mediates hormone-dependent transcriptional inhibition, perhaps via interaction with these or other accessory factors.

>> s l10 and drug?

4 FILES SEARCHED...

L12 1 L10 AND DRUG?

>> d

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS

AN 1999:355792 CAPLUS

DN 131:14490

TI Nuclear thyroid receptor ligand modeling based on three-dimensional structures of their ligand-binding domains

IN Scanlan, Thomas S.; Baxter, John D.; ***Fletterick, Robert J.*** ; Wagner, Richard L.; Kushner, Peter J.; Apriletti, James W.; West, Brian L.; Shiau, Andrew K.

PA The Regents of the University of California, USA

SO PCT Int. Appl., 447 pp.

CODEN: PIXXD2

DT Patent

LA English

FAM.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926966	A2	19990603	WO 1998-US25296	19981125
WO 2000026966	A3	20000120		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9917999	A1	19990615	AU 1999-17999	19981125
PRAI US 1997-980115		19971126		
WO 1998-US25296		19981125		
OS MARPAT 131:14490				

>> s l10 and coactivator?

AB Combinatorial regulation of transcription implies flexible yet precise assembly of multiprotein regulatory complexes in response to signals. Biochem. and crystallog. anal. revealed that hormone binding leads to the formation of a hydrophobic groove within the ligand-binding domain (LBD) of the thyroid hormone receptor that interacts with an LXXLL motif-contg. .alpha.-helix from GRIP1, a ***coactivator***. Residues immediately adjacent to the motif modulate the affinity of the interaction; the motif and the adjacent sequences are employed to different extents in binding to different receptors. Such interactions of amphipathic .alpha.-helices with hydrophobic grooves define protein interfaces in other regulatory complexes as well. We suggest that these common structural elements impact flexibility to combinatorial regulation, whereas side chains at the interface impart specificity.

TI Structure and specificity of nuclear receptor- ***coactivator*** interactions

AU Darimont, Beatrice D.; Wagner, Richard L.; Apriletti, James W.; Stallcup, Michael R.; Kushner, Peter J.; Baxter, John D.; ***Fletterick, Robert*** J.*** ; Yamamoto, Keith R.

AB . . . within the ligand-binding domain (LBD) of the thyroid hormone receptor that interacts with an LXXLL motif-contg. .alpha.-helix from GRIP1, a ***coactivator***. Residues immediately adjacent to the motif modulate the affinity of the interaction; the motif and the adjacent sequences are employed. . . .

IT Transcription factors

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process) (GRIP1 (glucocorticoid receptor-interacting protein-1); structure and specificity of thyroid hormone receptor- ***coactivator*** GRIP1 interactions)

IT Protein motifs

(ligand-binding domain and LXXLL motif; structure and specificity of thyroid hormone receptor- ***coactivator*** GRIP1 interactions)

IT Nuclear receptors

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process) (structure and specificity of nuclear receptor- ***coactivator*** interactions)

IT Transcriptional regulation

.alpha.-Helix (protein conformation)

(structure and specificity of thyroid hormone receptor- ***coactivator*** GRIP1 interactions)

IT Thyroid ***hormone*** ***receptor*** .beta.

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process) (structure and specificity of ***thyroid*** hormone receptor- ***coactivator*** GRIP1 interactions)

IT 6893-02-3, Triiodothyronine

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(structure and specificity of thyroid hormone receptor- ***coactivator*** GRIP1 interactions)

L13 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2000 ACS

TI Mechanisms of thyroid hormone action: insights from X-ray crystallographic and functional studies

AU Ribeiro, Ralf C. J.; Apriletti, James W.; Wagner, Richard L.; West, Brian L.; Feng, Weijun; Huber, Russ; Kushner, Peter J.; Nilsson, Steffan; Scanlan, Thomas; ***Fletterick, Robert J.*** ; Schaefele, Fred; Baxter, John D.

SO Recent Prog. Horm. Res. (1998), Volume Date 1997, 53, 351-394

CODEN: RPHRA6; ISSN: 0079-9963

L13 5 L10 AND COACTIVATOR?

>> d 1

L13 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2000 ACS

AN 1998:761699 CAPLUS

DN 130:120377

TI Structure and specificity of nuclear receptor- ***coactivator*** interactions

AU Darimont, Beatrice D.; Wagner, Richard L.; Apriletti, James W.; Stallcup, Michael R.; Kushner, Peter J.; Baxter, John D.; ***Fletterick, Robert*** J.*** ; Yamamoto, Keith R.

CS Dep. Cellular and Mol. Pharmacology, Univ. California at San Francisco (UCSF), San Francisco, CA, 94143, USA

SO Genes Dev. (1998), 12(21), 3343-3356

CODEN: GEDEEP; ISSN: 0890-9369

PB Cold Spring Harbor Laboratory Press

DT Journal

LA English

RE.CNT 53

(1) Adams, P. Proc Natl Acad Sci 1997, V94, P5018 CAPLUS

(2) Anzick, S. Science 1997, V277, P965 CAPLUS

(3) Apriletti, J. Protein Expr Purif 1995, V6, P363 CAPLUS

(4) Barrett, D. EMBO J 1994, V13, P3039 CAPLUS

(5) Bourguet, W. Nature 1995, V375, P377 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2000 ACS

AN 1998:750997 CAPLUS

DN 130:119652

TI Mechanisms of thyroid hormone action: insights from X-ray crystallographic and functional studies

AU Ribeiro, Ralf C. J.; Apriletti, James W.; Wagner, Richard L.; West, Brian L.; Feng, Weijun; Huber, Russ; Kushner, Peter J.; Nilsson, Steffan; Scanlan, Thomas; ***Fletterick, Robert J.*** ; Schaefele, Fred; Baxter, John D.

CS Metabolic Research Unit, University of California, San Francisco, CA, 94143-0540, USA

SO Recent Prog. Horm. Res. (1998), Volume Date 1997, 53, 351-394

CODEN: RPHRA6; ISSN: 0079-9963

PB Endocrine Society

DT Journal: General Review

LA English

RE.CNT 194

(1) Andersson, M. Nucleic Acids Res 1992, V20, P4803 CAPLUS

(2) Apriletti, J. Protein Expr Purif 1995, V6(3), P363 CAPLUS

(3) Ballard, P. Glucocorticoid Hormone Action 1979, V12, P25 CAPLUS

(4) Banihmad, A. Cell 1990, V61, P505 CAPLUS

(5) Banihmad, A. Molec Cell Biol 1995, V15(1), P76 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2000 ACS

TI Structure and specificity of nuclear receptor- ***coactivator*** interactions

AU Darimont, Beatrice D.; Wagner, Richard L.; Apriletti, James W.; Stallcup, Michael R.; Kushner, Peter J.; Baxter, John D.; ***Fletterick, Robert*** J.*** ; Yamamoto, Keith R.

SO Genes Dev. (1998), 12(21), 3343-3356

CODEN: GEDEEP; ISSN: 0890-9369

AB A review, with .apprx.200 refs., on the mechanisms of thyroid hormone action over the past two decades. We have attempted to place our studies on thyroid hormone receptors (TRs) in perspective with the work conducted by other investigators that established their nuclear localization, DNA-binding properties, DNA response elements, and the role of other proteins involved in TR-mediated regulation of gene transcription. Recently, our crystallog. studies of the TR ligand binding domain (LBD) revealed that the ligand has a structural role in the folding of the receptor's hydrophobic core. The anal. of the structure led to biochem. and genetic studies that have defined the surfaces on the TR LBD required for dimerization and binding of ***coactivator*** proteins. Placement of the mutations found in patients with the syndrome of generalized resistance to thyroid hormone on the TR LBD revealed that they were restricted to amino acids in the vicinity of the binding pocket for thyroid hormone. The insights gained from the elucidation of the TR LBD structure will provide the basis for the design of compds. with selective agonistic or antagonistic activities.

AU . . . Apriletti, James W.; Wagner, Richard L.; West, Brian L.; Feng, Weijun; Huber, Russ; Kushner, Peter J.; Nilsson, Steffan; Scanlan, Thomas; ***Fletterick, Robert J.*** ; Schaefele, Fred; Baxter, John D.

AB . . . to biochem. and genetic studies that have defined the surfaces on the TR LBD required for dimerization and binding of ***coactivator*** proteins. Placement of the mutations found in patients with the syndrome of generalized resistance to thyroid hormone on the TR. . . .

IT Thyroid ***hormone*** ***receptors***

RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)

(***thyroid*** hormone mechanism insights from X-ray crystallog. and functional studies)

L13 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2000 ACS

TI Molecular and structural biology of thyroid hormone receptors

AU Apriletti, James W.; Ribeiro, Ralf C. J.; Wagner, Richard L.; Feng, Weijun; Webb, Paul; Kushner, Peter J.; West, Brian L.; Nilsson, Steffan; Scanlan, Thomas S.; ***Fletterick, Robert J.*** ; Baxter, John D.

SO Clin. Exp. Pharmacol. Physiol. (1998), 25(Suppl., Future Perspectives in Molecular Endocrinology), S2-S11

CODEN: CEXBP9; ISSN: 0305-1870

AB A review, with 45 refs. Thyroid hormone receptors (TR) are expressed from two sep. genes (.alpha. and .beta.) and belong to the nuclear receptor superfamily, which also contains receptors for steroids, vitamins and prostaglandins. Unliganded TR are bound to DNA thyroid hormone response elements (TRE) predominantly as homodimers, or as heterodimers with retinoid X-receptors (RXR), and are assoc. with a complex of proteins contg. corepressor proteins. Ligand binding promotes corepressor disassoc. and binding of a ***coactivator***. Recent studies from our group have focused on the acquisition and use of X-ray crystallog. structures of ligand-binding domains (LBD) of both the rat (r) TR.alpha. and the human (h) TR.beta. bound to several different ligands. We have also developed ligands that bind selectively to the TR.beta., which may provide ways to explore the differential functions of TR.alpha. compared with TR.beta. isoforms. The LBD is comprised mostly of .alpha.-helices. The ligand is completely buried in the receptor and forms part of its hydrophobic core. Kinetic studies suggest that the limiting step in formation of high-affinity ligand-receptor complexes is the rate of folding of the receptor around the ligand. Ligands can be fitted tightly in the ligand-binding pocket and small differences in this fitting may explain many structure-activity relationships. Interestingly, anal. of the structures of antagonists suggests that they have chem. groups, "extensions", that could impair receptor folding around them and, thus, prevent the agonist-induced conformation changes in the receptor. The TR

structures allowed us to see that the mutations occur in the syndrome of generalized resistance to thyroid hormone are located in the vicinity of the ligand-binding pocket. X-ray structure of the TR has also been used to guide construction of mutations in the TR surface that block binding of various proteins important for receptor function. Studies with these TR mutants reveal that the interfaces for homo- and heterodimerization map to similar residues in helix 10 and 11 and also allow the definition of the surface for binding of ***coactivators***, which appears to be general for nuclear receptors. Formation of this surface, which involves packing of helix 12 of the TR into a scaffold formed by helices 3 and 5, appears to be the major change in the receptor structure induced by hormone occupancy.

AU . . . C. J.; Wagner, Richard L.; Feng, Weijun; Webb, Paul; Kushner, Peter J.; West, Brian L.; Nilsson, Stefan; Scanlan, Thomas S.; Fletterick, Robert J.*** ; Baxter, John D.

AB . . . and are assoc. with a complex of proteins contg. corepressor proteins. Ligand binding promotes corepressor dissociation, and binding of a ***coactivator***. Recent studies from our group have focused on the acquisition and use of X-ray crystallog. structures of ligand-binding domains (LBD). . . map to similar residues in helix 10 and 11 and also allow the definition of the surface for binding of ***coactivators***, which appears to be general for nuclear receptors. Formation of this surface, which involves packing of helix 12 of the . . .

IT Thyroid ***hormone*** ***receptors***
 RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
 (***thyroid*** hormone receptor mol. and structural biol.)

L13 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2000 ACS

TI X-ray crystallographic and functional studies of thyroid hormone receptor

AU Ribeiro, Ralf C. J.; Apriletti, James W.; Wagner, Richard L.; Feng, Weijun; Kushner, Peter J.; Nilsson, Stefan; Scanlan, Thomas S.; West, Brian L.; Fletterick, Robert J.*** ; Baxter, John D.

SO J. Steroid Biochem. Mol. Biol. (1998), 65(1-6), 133-141
 CODEN: JSBBEZ; ISSN: 0960-0760

AB A review with 28 refs. We have solved several x-ray crystallog. structures of TR ligand-binding domains (LBDs), including the rat (r) TR.alpha. and the human (h) TR.beta. bound to diverse ligands. The TR-LBD folding, comprised mostly of .alpha.-helices, is likely to be general for the superfamily. The ligand, buried in the receptor, forms part of its hydrophobic core. Tight fitting of ligand into the receptor explains its high affinity for the TR, although the structure suggests that ligands with even higher affinities might be generated. The kinetics of 3,5,3'-triiodo-L-thyronine (T3) and 3,5,3',5'-tetraiodo-L-thyronine (T4) binding suggest that folding around the ligand, rather than receptor opening, is rate-limiting for high affinity binding. TR.beta. mutations in patients with resistance to T3 cluster around the ligand; these different locations could differentially affect other receptor functions and explain the syndrome's clin. diversity. Guided by the structure, mutations have been placed on the TR surface to define interactions with other proteins. They suggest that a similar surface in the LBD is utilized for homo- or heterodimerization on direct repeats and inverted palindromes but not on palindromes. ***Coactivator*** proteins that mediate TR transcriptional activation bind to a small surface comprised of residues on four helices with a well-defined hydrophobic cleft, which may be a target for pharmaceuticals. The ***coactivator*** -binding surface appears to form upon ligand-binding by the folding of helix 12 into the scaffold formed by helices 3, 4 and 5. The anal. of most currently used antagonists suggest that although they probably fit into the ligand-binding pocket, they possess a group that may alter proper folding of the receptor, with disruption of the ***coactivator***

disproportionately impaired relative to its ligand-binding affinity, whereas its T3-dependent recruitment of ***coactivator*** was unimpaired. These properties were shared by another previously described RTH mutant (R429Q), and in the crystal structure of TR.alpha. . .

IT Missense mutation
 (R383H; thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Promoter (genetic element)
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
 (TSH.alpha. and TRH; thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Thyroid ***hormones***
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (metabolic disorders, resistance syndrome; thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Transcriptional activation
 Transcriptional repression
 (thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Thyroid ***hormone*** ***receptor*** .beta.
 RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (***thyroid*** ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Retinoid X receptors
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT Endocrine diseases
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (thyroid ***hormone*** resistance syndrome; thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT 24305-27-9, Thyrotropin-releasing ***hormone***
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (gene promoter; thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT 6993-02-3, Triiodothyronine
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

IT 9002-71-5, Thyrotropin

-binding surface (the "extension model").

AU . . . J.; Apriletti, James W.; Wagner, Richard L.; Feng, Weijun; Kushner, Peter J.; Nilsson, Stefan; Scanlan, Thomas S.; West, Brian L.; Fletterick, Robert J.*** ; Baxter, John D.

AB . . . similar surface in the LBD is utilized for homo- or heterodimerization on direct repeats and inverted palindromes but not on palindromes. ***Coactivator*** proteins that mediate TR transcriptional activation bind to a small surface comprised of residues on four helices with a well-defined hydrophobic cleft, which may be a target for pharmaceuticals. The ***coactivator*** -binding surface appears to form upon ligand-binding by the folding of helix 12 into the scaffold formed by helices 3, 4. . . into the ligand-binding pocket, they possess a group that may alter proper folding of the receptor, with disruption of the ***coactivator*** -binding surface (the "extension model").

IT Thyroid ***hormone*** ***receptors***
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
 (X-ray crystallog. and functional studies of ***thyroid*** hormone receptor)

L13 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2000 ACS

TI A novel TR.beta. mutation (R383H) in resistance to thyroid hormone syndrome predominantly impairs corepressor release and negative transcriptional regulation

AU Clifton-Bligh, R. J.; De Zegher, F.; Wagner, R. L.; Collingwood, T. N.; Francois, I.; Van Helvoirt, M.; Fletterick, R. J.*** ; Chatterjee, V. K. K.

SO Mol. Endocrinol. (1998), 12(5), 609-621
 CODEN: MOENEN; ISSN: 0888-8809

AB Resistance to thyroid hormone (RTH) is characterized by elevated serum thyroid hormones, failure to suppress pituitary TSH secretion, and variable T3 responsiveness in peripheral tissues. The disorder is assocd. with diverse mutations that cluster within three areas of the thyroid hormone .beta. (TR.beta.) receptor. Here, the authors report a novel RTH mutation (R383H), which is located in a region not known to harbor naturally occurring mutations. Although the R383H mutant receptor activated pos. regulated genes to an extent comparable to wild-type (WT), neg. transcriptional regulation of human TSH.alpha. and TRH promoters was impaired in either TR.beta.1 or TR.beta.2 contexts, and WT receptor function was dominantly inhibited. T3-dependent changes in basal transcription with R383H were also impaired: on the TRH promoter, basal activation by unliganded R383H was not reversed by T3 to the same extent as WT; similarly transcriptional silencing by an unliganded Gal4-R383H fusion was not relieved at a T3 concn. that depressed WT. In keeping with this, ligand-dependent corepressor release by R383H, either in a protein-protein interaction assay or as a DNA-bound heterodimer with retinoid X receptor on either pos. or neg. thyroid hormone response elements, was disproportionately impaired relative to its ligand-binding affinity, whereas its T3-dependent recruitment of ***coactivator*** was unimpaired. These properties were shared by another previously described RTH mutant (R429Q), and in the crystal structure of TR.alpha. the homologous residues interact in a polar invagination. The authors' data indicate a role for these residues in mediating neg. transcriptional regulation and facilitating corepressor release and suggest that predominant impairment of these functions may be the minimal requirements for causation of RTH.

AU Clifton-Bligh, R. J.; De Zegher, F.; Wagner, R. L.; Collingwood, T. N.; Francois, I.; Van Helvoirt, M.; Fletterick, R. J.*** ; Chatterjee, V. K. K.

AB . . . pos. or neg. thyroid hormone response elements, was

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (.alpha.-subunit gene promoter; thyroid ***hormone*** ***receptor*** .beta. mutation (R383H) in human resistance to ***thyroid*** hormone syndrome predominantly impairs corepressor release and neg. transcriptional regulation)

=> file medline biosis caplus embase lifesci scisearch toxline

(FILE 'HOME' ENTERED AT 10:30:12 ON 12 JUN 2000)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, LIFESCI, SCISEARCH, TOXLINE'
ENTERED AT 10:31:44 ON 12 JUN 2000

L1 941825 S THYROID OR RETINOID OR PEROXISOME OR GLUCOCORTICOID OR PROGES
L2 2756052 S RECEPTOR? OR LBD OR (LIGAND (W) BINDING (W) DOMAIN?)
L3 1871 S STRUCTURE? (5W) DRUG (5W) DESIGN?
L4 13 S L1 AND L2 AND L3
L5 7 DUP REM L4 (6 DUPLICATES REMOVED)
L6 6 S (L1 (7W) L2) AND L3
L7 4 DUP REM L6 (2 DUPLICATES REMOVED)
L8 19783 S NUCLEAR (W) RECEPTOR?
L9 154177 S L1 (7W) L2
L10 2 S L9 AND L8 AND L3

=> a thyroid or retinoid or peroxisome or glucocorticoid or progestin or
mineralcorticoid or estrogen or icosanoid

5 FILES SEARCHED...

L1 941825 THYROID OR RETINOID OR PEROXISOME OR GLUCOCORTICOID OR PROGESTIN
OR MINERALCORTICOID OR ESTROGEN OR ICOSANOID

=> a receptor? or lbd or (ligand (w) binding (w) domain?)

4 FILES SEARCHED...

L2 2756052 RECEPTOR? OR LBD OR (LIGAND (W) BINDING (W) DOMAIN?)

=> a structure? (5w) drug (5w) design?

4 FILES SEARCHED...

L3 1871 STRUCTURE? (5W) DRUG (5W) DESIGN?

=> s l1 and l2 and l3

L4 13 L1 AND L2 AND L3

=> dup rem l4

PROCESSING COMPLETED FOR L4

L5 7 DUP REM L4 (6 DUPLICATES REMOVED)

=> d ti au so abs kwic 1-7

L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2000 ACS

TI NMR studies of protein-ligand and protein-protein interactions involving
proteins of therapeutic interest

AU Feeney, J.

SO NATO ASI Ser., Ser. C (1999), 526(NMR in Supramolecular Chemistry),
281-300

CODEN: NSCSDW; ISSN: 0258-2023

AB A review with 65 refs. Currently there is great interest in trying to
understand the mol. recognition processes involved in protein-ligand and
protein-protein interactions. Such interactions are of crucial importance
in many areas of biol. including enzyme catalysis and regulation, the
control of gene expression and in drug- ***receptor*** interactions.
In all cases the specificity of binding is central to the biol. function.
Much of our recent work has been aimed at trying to understand the mol.
basis for binding specificity in drug- ***receptor*** complexes where

AU Klaholz, Bruno P.; Moras, Dino

SO Pure Appl. Chem. (1998), 70(1), 41-47

CODEN: PACHAS; ISSN: 0033-4545

AB A review with 37 refs. Nuclear ***receptors*** play an important role in
transcription regulation. They bind as homo- or heterodimers to the
response elements of their target genes and interact with numerous and
diverse partners, e.g. coactivator and corepressor proteins, and
transcription factors. Many of these processes are ligand-dependent, i.e.
binding of natural ligands activates the nuclear ***receptor***
through conformational changes of the protein. Synthetic ligands can be
made specific for a particular ***receptor*** and have the potential
for reducing the side-effects of natural ligands in pharmaceutical
applications. The crystal structures of ***ligand*** - ***binding***
domains of the ***retinoid*** ***receptors*** have brought
the first insight into the spatial organization and the nature of the
ligand-induced changes at the at. level. Furthermore, these structures
provide a starting point for ***structure*** -based ***drug***
design of ***retinoids***.

TI A structural view of ligand binding to the ***retinoid***

receptors

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the first insight into the spatial organization and the nature of the
ligand-induced changes at the at. level. Furthermore, these structures
provide a starting point for ***structure*** -based ***drug***
design of ***retinoids***.

ST crystal structure ***ligand*** ***binding*** ***domain***

review: nucleus ***receptor*** ***retinoid*** ligand binding

review

IT Crystal structure
(of ***ligand*** - ***binding*** ***domains*** ; structural
view of ligand binding to ***retinoid*** ***receptors***)

IT Cell nucleus

Molecular association

Transcriptional regulation

(structural view of ligand binding to ***retinoid***

receptors)

IT Ligands

Retinoids

RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BIOL (Biological study); PROC (Process)

(structural view of ligand binding to ***retinoid***

receptors)

IT ***Retinoid*** ***receptors***

RL: BPR (Biological process); PRP (Properties); BIOL (Biological study);
PROC (Process)

(structural view of ligand binding to ***retinoid***

receptors)

L5 ANSWER 3 OF 7 MEDLINE

DUPLICATE 2

TI Solution structures of the melanocyte-stimulating hormones by
two-dimensional NMR spectroscopy and dynamical simulated-annealing
calculations.

the findings can have practical significance by providing the basis for
rational ***structure*** -based ***drug*** ***design***. The
NMR method is well-suited to studies of such systems in soln. and we have
been applying NMR and other spectroscopic techniques, together with mol.
modeling and biochem. approaches, to characterize the structures and
ligand interactions in several complexes. Our specific aims are first, to
det. the soln. structures of specific proteins and their complexes and to
detect and characterize any mixts. of conformations and, second, to
investigate the specificity of binding by identifying and characterizing
individual interactions between the ligand and protein and measuring the
rates of dynamic processes within the complexes. Some of the complexes
studied are sufficiently small (less than 35 kDa) to allow detailed
structural work to be carried out in soln. For example, we have detd. the
structures of several complexes of Lactobacillus casei dihydrofolate
reductase (162 residues) with antifolate drugs and used NMR measurements
to characterize specific interactions, conformational equil. and dynamic
processes within the complexes. However, many other proteins of
therapeutic interest form complexes that are too large for complete
structural detn. by NMR. In such cases an alternative approach is to
examine smaller domains of the proteins which have retained their
structural and functional properties. In some cases, studies of complexes
formed by functional domains of large proteins can also provide useful
information and we have used this approach to examine interactions
involving matrix metalloproteinases and their inhibitors (for example
tissue inhibitors of metalloproteinases, TIMPs). We have carried out
structural detns. on a truncated form of one of these, A-TIMP-2, and
defined its interaction surface in the complex formed with a 19 kDa
catalytic domain from stromelysin. There are many other proteins for
which ***receptors*** have not yet been isolated. In these cases
structural information can be obtained for the known partner and used, in
combination with data from mutagenesis and functional studies, to probe
its binding sites for a putative ***receptor***. Such approaches have
been used in our structural studies of trefol proteins such as PSP
(pancreatic spasmolytic polypeptide) and pNR-2/ps2 (a breast cancer
assocd. trefol protein).

AB . . . of crucial importance in many areas of biol. including enzyme
catalysis and regulation, the control of gene expression and in drug-
receptor interactions. In all cases the specificity of binding is
central to the biol. function. Much of our recent work has been aimed at
trying to understand the mol. basis for binding specificity in drug-
receptor complexes where the findings can have practical
significance by providing the basis for rational ***structure*** -based
drug ***design***. The NMR method is well-suited to studies
of such systems in soln. and we have been applying NMR and other. . .
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structural studies of trefol proteins such as PSP (pancreatic spasmolytic
polypeptide) and pNR-2/ps2. . .
IT Proteins, specific or class
RL: PRP (Properties)
(p52, ***estrogen*** -induced; NMR studies of protein-ligand and
protein-protein interactions involving proteins of therapeutic
interest)

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2000 ACS

DUPLICATE 1

TI A structural view of ligand binding to the ***retinoid***

receptors

AU Lee J H; Lim S K; Huh S H; Lee D; Lee W

SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1998 Oct 1) 257 (1) 31-40.

Journal code: EMJ; ISSN: 0014-2956.

AB Melanocortins, which are involved in melanocyte pigmentation control and
glucocorticoid stimulation, have functional roles in various
physiological mechanisms and have been shown to participate in higher
cortical functions. Recently, it has also been reported that
melanocyte-stimulating hormone (MSH) and melanocortin 4 ***receptor***
(MC4R) are the key components of the hypothalamic response to obesity. The
solution structures of both melanocyte-stimulating hormone alpha-MSH
(Ac-Ser-Tyr-Ser-Met-Glu-His-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH2) and its
analog alpha-MSH-ND (Ac-Ahx-Asp-His-DPhe-Arg-Trp-Lys-NH2) (Ahx,
2-aminohexanoic acid) have been determined by two-dimensional NMR
spectroscopy and simulated-annealing calculations. The NMR data revealed
that alpha-MSH forms a hairpin loop conformation which includes conserved
message sequences, whereas alpha-MSH-ND prefers a type I beta-turn
comprising residues of Asp2-His3-DPhe4-Arg5. Final simulated-annealing
structures of both alpha-MSH-ND and alpha-MSH peptides converged with r.m.s.d
of 0.07 nm for alpha-MSH-ND and 0.1 nm for alpha-MSH between backbone
atoms, respectively. This result will provide the structural bases of
melanocortin functions as well as valuable information for
structure -based ***drug*** ***design*** involving the
regulation of obesity and feeding.

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structural bases of melanocortin functions as well as valuable information
for ***structure*** -based ***drug*** ***design*** involving the
regulation of obesity and feeding.

L5 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2000 BIOSIS

TI Study on the structure-activity relationships of ***retinoids*** : II.

3D-QSAR of ***retinoids*** and ***receptor*** interaction.

AU Wang, W. M.; Huang, N.; Yang, G. Z.; Guo, Z. R.

SO Yaoxue Xuebao, (1997) Vol. 32, No. 1, pp. 43-48.

ISSN: 0513-4870.

AB Precise prediction of the binding constant of ligand to ***receptor***
is an important aspect of ***structure*** -based ***drug***
design. Almost all methods including de novo design and 3D
database search are over concentrated on structure generation rather than
quantitative evaluation of the binding properties of the newly produced
molecule. Using epididymal retinoic acid binding protein (ERABP) as a
model, we simulated the interaction between ***retinoids*** and their
receptor with DOCK program and obtained an equation for predicting
the binding constants. According to the docking conformers of the ligands,
CoMFA was also used to deduce a pharmacophoric model of this series of
compound.

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IT Miscellaneous Descriptors
BIOCHEMISTRY AND BIOPHYSICS; DOCK COMPUTER PROGRAM; PHARMACOLOGY; RETINOIC ACID BINDING PROTEIN; ***RETINOID*** - ***RECEPTOR*** INTERACTIONS; ***RETINOID*** ; 3-DIMENSIONAL QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIPS; 3D-QSAR

L5 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2000 ACS
TI Computer assisted drug design and biotechnology: a case study on lead optimization related to breast cancer therapy
AU Nilsson, S.; Norinder, U.
SO Bioact. Compd. Des. (1996), 109-118. Editor(s): Ford, Martyn G. Publisher: Bios Scientific Publishers, Oxford, UK.
CODEN: 63SXAI

AB A review with 24 refs. Nuclear steroid/ ***thyroid*** hormone ***receptors*** are key factors in the endocrine signalling pathways and they are assocd. with major clin. indications which highlights these effectors as important targets for drug design and drug development. Recent advances in our mechanistic understanding how these intracellular ***receptors*** function has led to an increased interest in discovery and development of novel synthetic hormonal drugs which can modulate their function and activity. The development and use of in vitro cellular based test systems for screening and anal. of natural and synthetic hormonal compds. for their agonistic and/or antagonistic activity in combination with computer assisted drug design we believe will facilitate the development of improved therapeutic agents.

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IT Biotechnology
Breast tumor inhibitors
Computer application
Drug design
Structure -activity relationship
(computer assisted ***drug*** ***design*** and biotechnol.: lead optimization related to breast cancer therapy)

IT Hormone ***receptors***
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(computer assisted drug design and biotechnol.: lead optimization related to breast cancer therapy)

L5 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2000 ACS
TI NMR studies of ***retinoid*** -protein interactions: The conformation of [13C2]-.beta.-ionone bound to .beta.-lactoglobulin B.
AU Sundaram, A. K.; Curley, R. W. Jr.; Fowble, J. W.; Abildgaard, F.; Westler, W. M.; Markley, J. L.
SO Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24 (1995), Issue Pt. 2, MEDI-225 Publisher: American Chemical Society, Washington, D. C.
CODEN: 61XGAC

AB NMR Spectroscopy has been used for studying the conformations of ***receptor*** -bound ligands and has become a useful tool for ***structure*** -based ***drug*** ***design***. Retinoic acid and its analogs are being studied as cancer chemopreventive agents. It

has been found that the actions of ***retinoids*** are mediated through assocn. with a no. of transport and ***receptor*** proteins. In recent years, it has been shown that the milk protein .beta.-lactoglobulin B binds ***retinoids*** with reasonably high affinity, resembles other ***retinoid*** binding proteins, and may serve as a good model for NMR studies of ***retinoid*** -protein interaction. We have prepd. a 13C-labeled retinol analog, .beta.-ionone (1) and used it as the ligand in isotope-edited NMR studies to identify its .beta.-lactoglobulin B-bound conformation. The result of our studies emphasizing the HMQCNOE expt. suggest that 1 binds as a 6-s-cis conformer. The synthesis of labeled 1, the exptl. details of the isotope-edited NMR studies, and implications for drug design will be presented.

TI NMR studies of ***retinoid*** -protein interactions: The conformation of [13C2]-.beta.-ionone bound to .beta.-lactoglobulin B.
AB NMR Spectroscopy has been used for studying the conformations of ***receptor*** -bound ligands and has become a useful tool for ***structure*** -based ***drug*** ***design***. Retinoic acid and its analogs are being studied as cancer chemopreventive agents. It has been found that the actions of ***retinoids*** are mediated through assocn. with a no. of transport and ***receptor*** proteins. In recent years, it has been shown that the milk protein .beta.-lactoglobulin B binds ***retinoids*** with reasonably high affinity, resembles other ***retinoid*** binding proteins, and may serve as a good model for NMR studies of ***retinoid*** -protein interaction. We have prepd. a 13C-labeled retinol analog, .beta.-ionone (1) and used it as the ligand in isotope-edited NMR studies. . .

L5 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 3
TI STEROID ***RECEPTOR*** ***STRUCTURE*** AND ANTIHORMONE ***DRUG*** ***DESIGN***
AU AGARWAL M K
SO Biochem. Pharmacol., (1992) 43 (11), 2299-2306. CODEN: BCPA6. ISSN: 0006-2952.
TI STEROID ***RECEPTOR*** ***STRUCTURE*** AND ANTIHORMONE ***DRUG*** ***DESIGN***
IT Miscellaneous Descriptors
HUMAN MINERALOCORTICOID ***RECEPTOR*** ***GLUCOCORTICOID*** ***RECEPTOR*** COMPLEMENTARY DNA MESSENGER RNA GENETIC ENGINEERING

(FILE 'HOME' ENTERED AT 10:30:12 ON 12 JUN 2000)
FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, LIFESCI, SCISEARCH, TOXLINE' ENTERED AT 10:31:44 ON 12 JUN 2000

L1 941825 S THYROID OR RETINOID OR PEROXISOME OR GLUCOCORTICOID OR PROGES
L2 2756052 S RECEPTOR OR LBD OR (LIGAND (W) BINDING (W) DOMAIN?)
L3 1871 S STRUCTURE? (SW) DRUG (SW) DESIGN?
L4 13 S L1 AND L2 AND L3
L5 7 DUP REM L4 (6 DUPLICATES REMOVED)

=> s (l1 (7w) l2) and l3
L6 6 (l1 (7w) l2) AND L3
=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 4 DUP REM L6 (2 DUPLICATES REMOVED)
=> d ti au so kwic l-4

L7 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
TI A structural view of ligand binding to the ***retinoid*** ***receptors***
AU Klaholz, Bruno P.; Moraes, Dino
SO Pure Appl. Chem. (1998), 70(1), 41-47
CODEN: PACHAS; ISSN: 0033-4545
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IT Crystal structure
(of ligand-binding domains; structural view of ligand binding to ***retinoid*** ***receptors***)
IT Cell nucleus
Molecular association
Transcriptional regulation
(structural view of ligand binding to ***retinoid*** ***receptors***)
IT Ligands
Retinoids
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
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RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(structural view of ligand binding to ***retinoid*** ***receptors***)

L7 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS
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IT Biotechnology
Breast tumor inhibitors
Computer application
Drug design
Structure -activity relationship
(computer assisted ***drug*** ***design*** and biotechnol.: lead optimization related to breast cancer therapy)

L7 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 2
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L4 13 S L1 AND L2 AND L3
L5 7 DUP REM L4 (6 DUPLICATES REMOVED)
L6 6 S (l1 (7w) l2) AND L3
L7 4 DUP REM L6 (2 DUPLICATES REMOVED)

=> s nuclear (w) receptor?
L8 19783 NUCLEAR (W) RECEPTOR?
=> s l1 (7w) l2
L9 154177 L1 (7w) L2
=> s l9 and l8 and l3
L10 2 L9 AND L8 AND L3
=> dup rem l10
PROCESSING COMPLETED FOR L10
L11 1 DUP REM L10 (1 DUPLICATE REMOVED)

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
AN 1998:345233 CAPLUS

DN 129:105561
TI A structural view of ligand binding to the ***retinoid***
receptors
AU Klaholz, Bruno P.; Moras, Dino
CS Lab. Biol. Struct., Inst. Genet. Biol. Mol. Cell., Ilkirsch, 67404, Fr.
SO Pure Appl. Chem. (1998), 70(1), 41-47
CODEN: PACHAS; ISSN: 0033-4545
PB Blackwell Science Ltd.
DT Journal: General Review
LA English

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
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IT Crystal structure
(of ligand-binding domains: structural view of ligand binding to ***retinoid*** ***receptors***)
IT Cell nucleus
Molecular association
Transcriptional regulation
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IT Ligands
Retinoids
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(structural view of ligand binding to ***retinoid***

(of ***ligand*** - ***binding*** ***domains*** ; structural view of ligand binding to retinoid ***receptors***)
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(structural view of ligand binding to retinoid ***receptors***)

L13 ANSWER 2 OF 2 LIFESCI COPYRIGHT 2000 CSA
TI Steroid ***receptor*** ***structure*** and antihormone
drug ***design***
AU Agarwal, M.K.
SO BIOCHEM. PHARMACOL., (1992) vol. 43, no. 11, pp. 2299-2306.
TI Steroid ***receptor*** ***structure*** and antihormone
drug ***design***
AB This article will review the structure/function basis of ***receptor***-mediated steroid hormone action as a prelude to the development of specific derivatives endowed with antagonist activity. The action of leading. . .
UT reviews; steroid hormones; ***nuclear*** ***receptors*** ; structure-activity relationships; drugs; antagonists

L13 ANSWER 2 OF 2 LIFESCI COPYRIGHT 2000 CSA
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drug ***design***
AU Agarwal, M.K.
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receptors)
IT ***Retinoid*** ***receptors***
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(structural view of ligand binding to ***retinoid***
receptors)

=> d hist

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L8 19783 S NUCLEAR (W) RECEPTOR?
L9 154177 S L1 (7W) L2
L10 2 S L9 AND L8 AND L3
L11 1 DUP REM L10 (1 DUPLICATE REMOVED)

=> s 18 and 12 and 13

L12 3 L8 AND L2 AND L3

=> dup rem 112

PROCESSING COMPLETED FOR L12
L13 2 DUP REM L12 (1 DUPLICATE REMOVED)
=> d ti au so kwic 1

L13 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
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SO Pure Appl. Chem. (1998), 70(1), 41-47
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ST crystal structure ***ligand*** ***binding*** ***domain***
review; nucleus ***receptor*** retinoid ligand binding review
IT Crystal structure